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ARCHIVES OF PEDIATRICS

A MONTHLY DEVOTED TO THE

DISEASES OF INFANTS AND CHILDREN

JOHN FITCH LANDON, M.D., Editor

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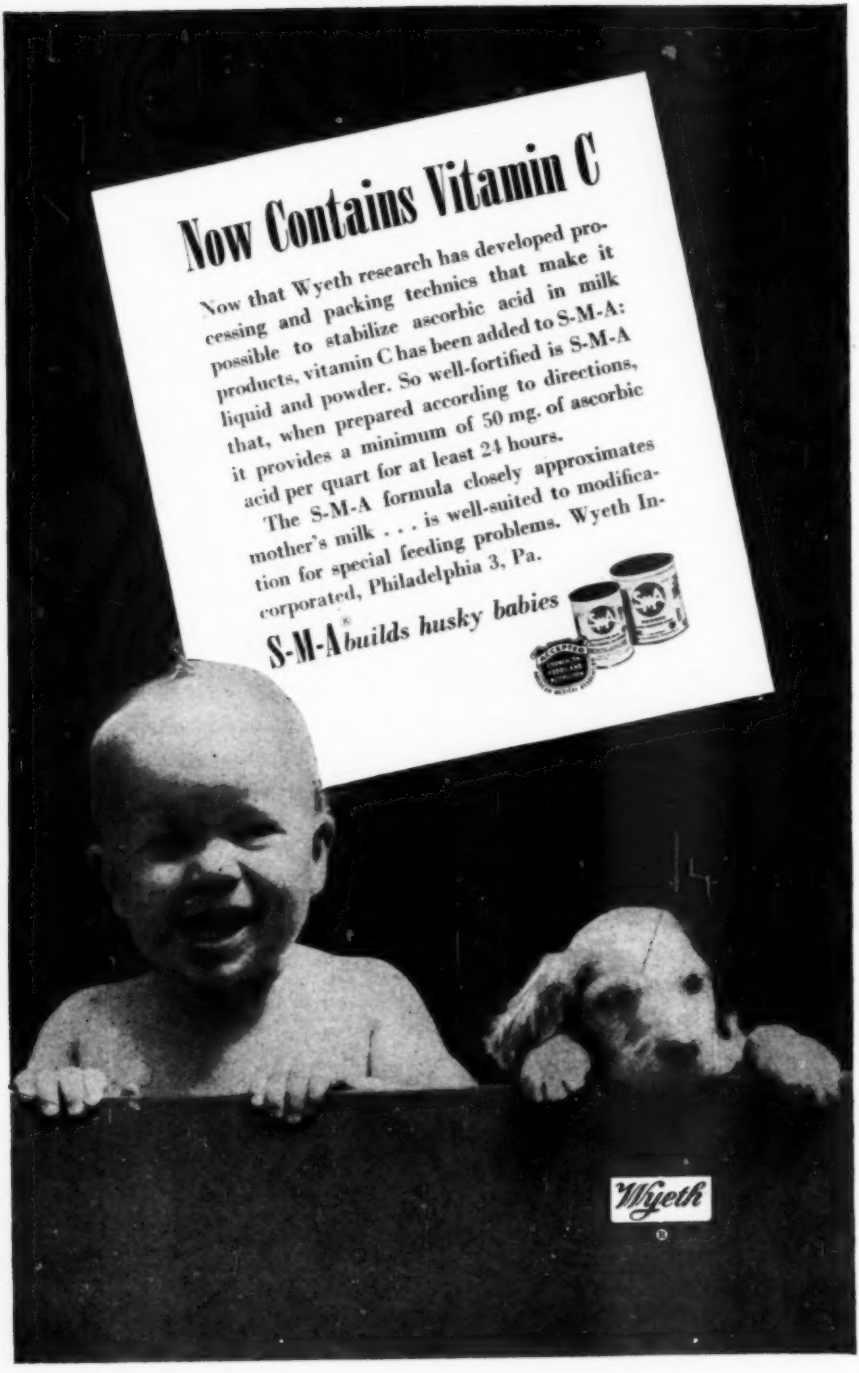
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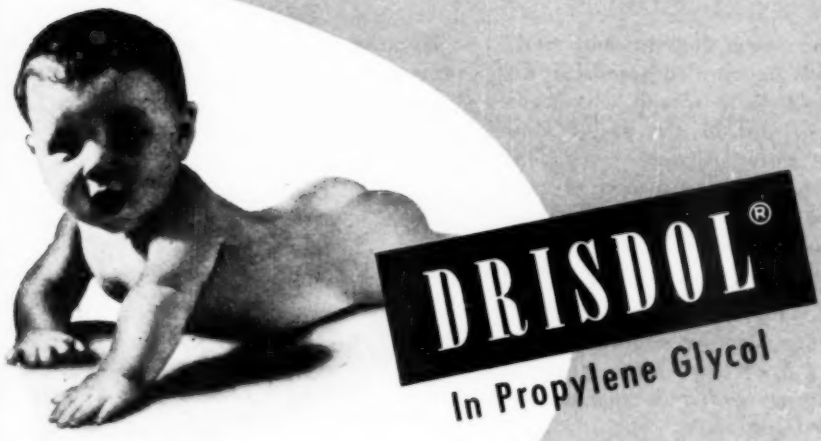

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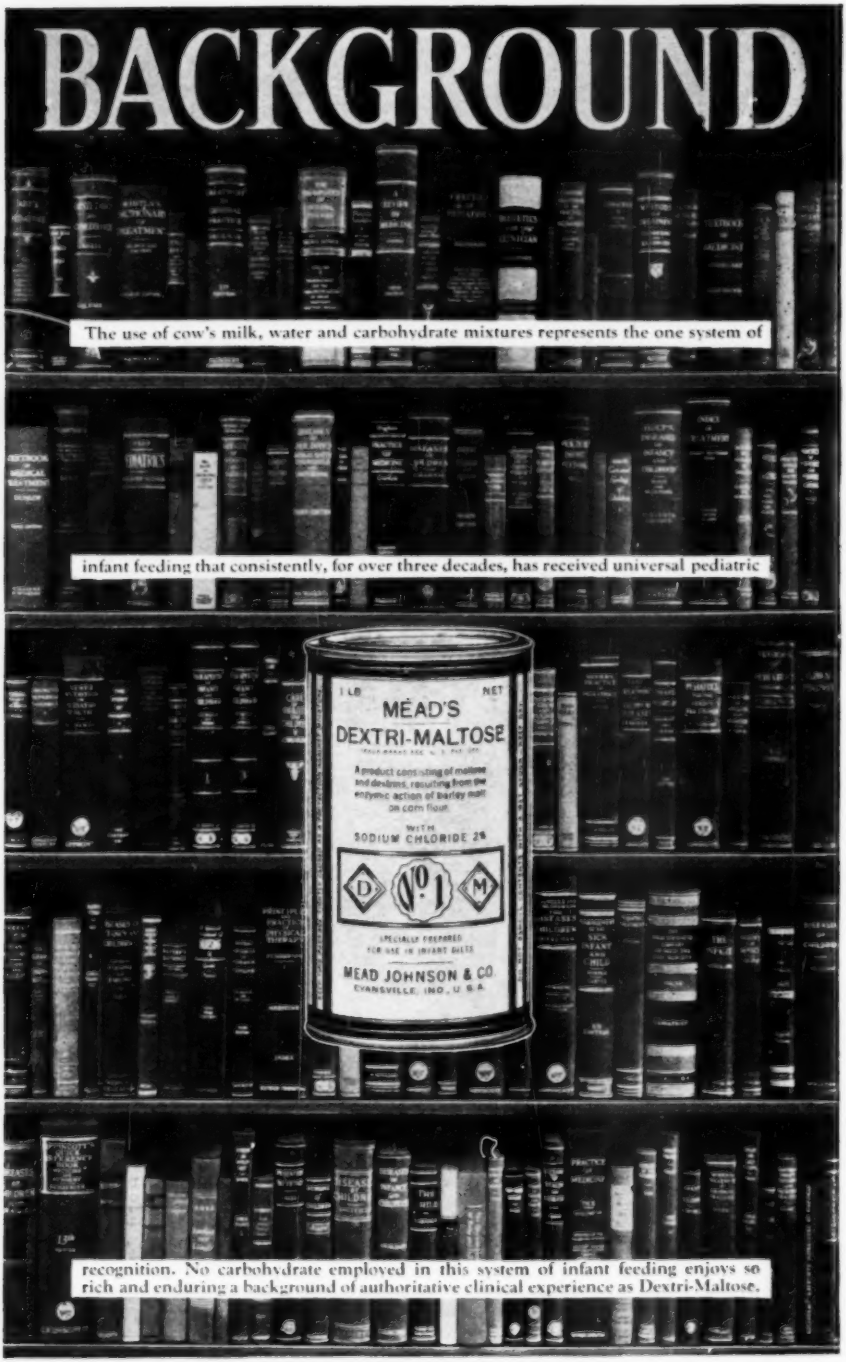
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FETAL PERITONITIS

REPORT OF FOUR CASES

BRUCE F. GROTTS, M.D.

Milwaukee.

Abt, in 1931, could find only 85 reported cases of fetal peritonitis, and up to that time only one patient is known to have survived.[1, 2] In 1934, Davenport reported a case which survived after an operation on the third day of life. Since that time only isolated cases have been reported, with only occasional recoveries.[3-6]

In the past, fetal peritonitis was usually attributed to syphilis or tuberculosis, or was secondary to umbilical infection, occurring epidemically in lying-in hospitals.[7] Today, these causes are not usually responsible.

The reports of four cases of fatal fetal peritonitis, seen at Milwaukee Children's Hospital from 1943 to 1948, follow.

CASE REPORTS

Case 1. N. C., a female infant, was admitted to the hospital several hours after birth on August 3, 1943. The details of her birth and the maternal history were unobtainable. At the time of admission the baby was acutely ill and she cried constantly. The abdomen was enlarged and a rapid increase in size was observed. It was tympanitic to percussion in the upper quadrants but dull in the lower quadrants, and there was noticeable venous distention. When a catheter was passed into the stomach a greenish material was obtained, but a rectal catheter could not be passed beyond the sigmoid.

On the day of admission an exploratory operation was per-

formed, and an accidental colostomy resulted. An unsuccessful attempt was made to pass a catheter through this opening into the distal loop, and, following barium sulfate instillation, it appeared that there was a mass in the lower abdomen obstructing this loop. Shortly after the operation the patient died, the temperature climbing steadily from 100° F. on admission to 103° F. before death. No bowel movements occurred during her brief hospitalization.

Laboratory. The urine showed four plus albumin and an occasional W.B.C. The blood contained 25,130 leukocytes per cmm. with 43 per cent neutrophils, 43 per cent lymphocytes, 25 normoblasts per 100 W.B.C. and 17 grams of hemoglobin per 100cc.

At autopsy, the lungs appeared hemorrhagic and congested, with a small area of pneumonia in the right upper lobe. The other significant findings were limited to the gastro-intestinal tract.

The rectum, sigmoid and colon were small, contracted and empty. Forty centimeters from the cecum the bowel passed through an adhesion extending from the duodenum to the left peritoneal wall. Beyond this there appeared to be a volvulus, and the bowel proximal to this adhesion was considerably dilated with meconium. Still more proximally, the bowel was again kinked about the adhesion and it was into this dilated loop that the colostomy opening had been made. The twisting, however, had not appreciably interfered with the circulation.

Microscopically, both the liver and spleen contained recently hemolyzed blood. The pancreatic acini were atrophic, the stroma appeared more dense than normal, and the pancreatic duct appeared to be obstructed.

Case 2. J. L., a female infant, was 13 hours old when admitted on March 9, 1946. The child was born at full term and the labor had been normal. The infant's abdomen, however, had seemed distended at birth. The child was cyanotic, required oxygen, and was therefore transferred to Children's Hospital.

On examination, the baby had a weak cry but was not dyspneic. The abdomen was greatly distended and showed increased venous markings. It had a doughy feel and was dull to percussion in the lower quadrants, but tympanitic in the upper quadrants. The admission temperature was 100.5° F. which fell to normal within the next 12 hours and then rose to 100.5° F. again.

The following day she began to regurgitate meconium-like material, and her abdomen became more distended. Generalized edema and ascites were noted at this time.

By x-ray there was no evidence of obstruction of the stomach or small intestine. However, there were small soft areas of calcification to the left of the stomach as well as in the midabdomen. The kidney shadows could not be made out, and it was assumed this was due to the hydroperitoneum. A barium enema revealed a normal colon. Further studies were not completed, as the patient suddenly died on March 11, 1946.

Laboratory. A urine examination was not done, and the infant passed no stools. The W.B.C. count was 13,600 per cmm. with 37 per cent neutrophils, 45 per cent lymphocytes, and 30 normoblasts per 100 W.B.C. There were 3.32 million R.B.C. per cmm. and 11 grams of hemoglobin per 100 cc., and the Kline test was negative. An abdominal paracentesis, the day before death, produced 50 cc. of odorless greenish-yellow fluid which on culture was found to contain pneumococci and E. coli.

A post-mortem examination was not permitted.

Case 3. C. C., a female infant, was admitted six hours after birth on May 3, 1946. The maternal and birth histories were unobtainable.

On examination the child did not appear acutely ill. Her abdomen, however, was greatly distended, and on percussion was tympanitic. No masses could be felt, however. The rectal examination revealed no lesion, and a meconium stool followed this examination.

The following day a roentgenogram revealed gas in the stomach and small intestines, ascites, and flaky calcium deposits scattered throughout the abdomen.

In the hospital the infant did not tolerate oral feedings well, and was maintained on parenteral fluids. A Wangensteen tube was passed but did not decrease the distention, and parenteral administration of sulfadiazine was initiated. Three days after admission, 700 cc. of turbid yellow fluid was removed by abdominal pararcentesis, and hemolytic staphylococcus aureus and E. coli were isolated. Penicillin, in addition to the sulfadiazine, was then given. Repeated paracentesis on May 9 and May 15, 1946 revealed the same organisms, numerous W.B.C. and a positive test

for globulin (Rivalta test). The temperature remained about normal with occasional elevations to 100° or 101° F., and the infant began to take small amounts of formula and to have normal bowel movements.

On her fifteenth hospital day, however, she began to bleed from the needle puncture sites, and did not respond to the parenteral administration of vitamin K. A prothrombin determination showed no coagulation in 15 minutes, so a blood transfusion was given. She did not respond to these measures, however, and became cyanotic and died on May 18, 1946, the sixteenth hospital day.

Laboratory. A urine analysis was not done. The blood contained 9,800 W.B.C. per cmm. with 37 per cent segmented leukocytes, 46 per cent lymphocytes, and 20 grams of hemoglobin per 100 cc. The coagulation time the day before death was fourteen minutes, and the bleeding time was one-half minute.

At autopsy, the various needle puncture wounds were the sites of old hemorrhage. There was superficial abdominal venous distention and the peritoneal cavity contained about 100 cc. of amber fluid containing fibrin and pus. The open abdomen showed only the anterior surface of the liver, stomach and spleen, the remainder of the abdominal contents being obscured by a membranous partition interpreted as a thickened and fibrotic great omentum. Behind this partition the other viscera were found, all of which were involved in an adhesive peritonitis. There were calcium deposits in the great omentum and several segments of the mesentery. There were also several small nodules over the dome of the right lobe of the liver, as well as small calcified granules extending along the body of the pancreas. The intestinal wall was only secondarily involved. No intestinal perforation could be found, and there appeared to be no meconium in the small bowel or peritoneum.

Microscopically, there were fibrous adhesions and chronic inflammatory cells about the liver, and the nuclei of the liver cells varied considerably in size and in staining reaction, probably indicating parenchymatous liver injury of a diffuse type. Adhesions were present on the capsule of the spleen. On one surface of the thickened peritoneum the exudate was characteristic of acute peritonitis. In the pancreas there were inflammatory cells

about the ducts, interstitial fibrosis, and, in one section, acute necrosis. A section near the ampulla of Vater contained inspissated bile, and there was considerable peripancreatic fibrosis. The intestine was not remarkable, except where it was impinged upon from the outside by fibrous tissue and calcified areas.

Case 4. S. K. was a male infant, 48 hours old when admitted on May 9, 1947. Delivery had been normal, and the maternal history was noncontributory. He was dyspneic the first twenty-four hours of life, and had been kept in oxygen for this reason. He had refused food the first day and had vomited his feedings the second day.

On examination, the abdomen was distended and he seemed to have bilateral indirect inguinal hernias. There was edema of the right inguinal region and of the extensor surfaces of the lower extremities. No peristalsis was heard, and rectal examination revealed no lesion.

The initial roentgen examination revealed a loop of small bowel in the scrotum, and some distention of the small intestine. There was no gas in the colon. After initiation of Wangensteen suction a barium enema was given, and a thin string-like nonobstructed colon was identified. The small bowel had been decompressed, but the entire abdomen was hazy, indicating the presence of fluid.

The patient received supportive therapy, and his temperature was only 98° F. rectally, but he died suddenly within 12 hours after admission.

Laboratory. No urine was obtained, and the infant had no bowel movements. There were 11,200 W.B.C. per cmm. with 57 per cent neutrophils and 32 per cent lymphocytes, and 22.5 grams of hemoglobin per 100 cc.

On post-mortem examination the peritoneum contained a moderate amount of cloudy, yellow, fibrin-containing fluid, which showed E. coli on culture. There were numerous fibrous adhesions binding the intestines together, and connecting them with the parietal peritoneum. These adhesions were most marked in the right lower quadrant. The surfaces of the liver and spleen were covered with an inflammatory exudate. Three centimeters proximal to the ileocecal valve there was a definite narrowing of the terminal ileum. Its circumference was about half that of the adjacent bowel. However, there was yellow fecal material above and below this constriction.

On microscopic examination there was intense splenic congestion and some fatty degeneration of the liver. The liver also showed edema and congestion of the capsule and organizing perihepatitis. The wall of the small intestine seemed thickened and there was chronic and acute inflammation in the subserous layers. The pancreas appeared normal.

COMMENTS

Fetal peritonitis may cause death in utero, or the patient may die shortly after birth, the actual perforation, if present, taking place during labor. The earliest time of onset, however, cannot be determined with accuracy. Autopsies of still-born infants occasionally show the results of aseptic peritonitis in the form of adhesions and bands of connective tissue, often with matting of the intestines, even to the point of obscuring the exact relations of the abdominal viscera.[8] In our first case, for example, the findings could be interpreted as indicating aseptic fetal peritonitis associated possibly with early fetal development when the intestine was outside the abdominal cavity. This adhesive peritonitis resulted in obstruction due to a segregation of a portion of the small bowel by a fibrous omental adhesion. The pancreatic findings were suggestive of early fibrocystic disease, also possibly dependent upon intra-uterine infection.

Within a few hours after birth the intestine is invaded by bacteria and, then, if rupture occurs, true bacterial peritonitis follows. In about one-half of the cases reported there is a gross rupture of the intestine or stomach due to injury following strangulation or thinning of the intestine proximal to a stenotic segment.[9, 10] Almost every type of intestinal occlusion has been described, and bands and adhesions are present in almost every case, although whether these are primarily developmental or secondary to earlier perforation or placental transmission of inflammatory substances cannot be determined.[8, 11]

Sometimes, the site of rupture cannot be found, as in our cases, and malformations are not always present. S. K. (Case 4), apparently, represented a case of intra-uterine peritonitis with peritoneal adhesions and constriction of the ileum. The source of perforation was not found, however, but the etiological agent was identified as E. coli.

Trauma, intestinal infection, vascular insufficiency, congenital diverticula, appendicitis, gastric or duodenal ulcers, and angulation or kinks in the bowel, are also cited as causes of perforation.[12, 13]

In Landsteiner's and Kornblith's cases the obstruction appeared to be due to inspissated meconium.[9] The term meconium peritonitis, however, is applicable only to cases in which meconium, calcified meconium, mucous droplets, foreign body giant cells, and fibrous or fibrinous adhesions are found in the peritoneum.[14] Meconium plaques, when present, may calcify early according to Boikan, even within 24 hours. Case 2, for example, at 13 hours of age, showed calcified plaques on the x-ray film (as did Case 3), and it seems likely that this infant had a meconium peritonitis with calcification of some meconium plaques in utero, followed secondarily by bacterial invasion.

A few cases of meconium obstruction have been reported, several with fibrosis of the pancreas and cystic dilatation of the pancreatic ducts, similar to our first case.[15, 16] The meconium peritonitis may be secondarily infected with staphylococci or streptococci, as in Case 2, and occasionally the peritonitis is entirely bacterial, following intestinal rupture or septicemia or placental transmission of bacteria.[9] In these cases, staphylococci, streptococci, E. coli, or pneumococci may be isolated.[17, 18] However, few bacteriologic studies have been recorded on any reported series.[13] In three of our four cases, cultures were done. In Case 2 pneumococci and E. coli were isolated, and in Case 3 hemolytic staphylococcus aureus and E. coli were obtained. Both cultures were made ante-mortem from paracentesis fluid. In Case 4, E. coli was obtained by post-mortem culture of the abdominal fluid.

Infants born with peritonitis usually are still-born or die shortly after birth. They may live to show signs of intestinal obstruction. The most striking and consistent symptom is rapid abdominal distention, and in some cases the distention becomes great enough before birth to cause dystocia. The infant is usually profoundly shocked, stools are not passed, and vomiting may be persistent. Often there is edema of the flanks and scrotum or vulva, ascites, and tympanites. There may be cyanosis and respiratory embarrassment due to diaphragmatic pressure, and free gas may be present

in the peritoneum. The temperature may be subnormal and the blood count has been found to be of little diagnostic value.[13]

The x-ray is of importance in early diagnosis, and, if a perforation is present, its site may be located by barium.[19] Neuhof, in discussing Donovan's paper on primary pneumococcus peritonitis, states that "diagnosis can always be made by abdominal puncture."[20]

The present high mortality may, in the future, be reduced by the use of the sulfonamides and antibiotics, if diagnosis and bacterial etiology are ascertained earlier. Surgical intervention offers the only chance with perforation or obstruction, but is rarely successful.[13,19]

SUMMARY

Four fatal cases of fetal peritonitis are recorded. They were associated with intestinal malformations, and/or cystic fibrosis of the pancreas.

Bacterial infection of the peritoneum may be primary or secondary. E. coli, pneumococci and staphylococci were isolated in our cases.

Characteristic of fetal peritonitis is early abdominal distention and vomiting. Calcified abdominal meconium plaques are often seen on the x-ray film.

Following earlier diagnosis, it is hoped that the new anti-infective agents will lead to more successful treatment of this condition.

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FRIEDLANDER'S BACILLUS MENINGITIS IN NEWBORNS*

Report of Case in One of Colored Premature Twins and Review of the Literature

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Although Friedlander's bacillus was discovered in 1882,[1] the first case of meningitis was not reported until 1888 when Weichselbaum[2] described it at post-mortem. As a cause of meningitis its incidence has been so rare that in an extensive review of Friedlander's bacillus infections,[1] over a period of seventy-five years in which almost every system was involved, meningitis was noted in only two per cent of the cases. More recently its rarity has been illustrated in several reports on meningitis in which, out of 1,388 cases,[3, 4] not one case of Friedlander's bacillus was listed, while out of 3,377 other cases,[5] 7 cases were due to this organism (.02 per cent). Others[6] agree that it is one of the less frequent causes of meningitis and in summarizing the cases reported in several large cities only .08 per cent[7] had been due to this organism.

In 1918, Barron[8] reviewed 19 cases of meningitis in newborns of which only one was caused by Friedlander's bacillus while another report,[9] of 60 cases in infants under 6 months of age, reported none due to this organism. Furthermore, in a recent review[7] of the literature, only 30 cases of Friedlander's bacillus meningitis were found, of which 11 were in children and five of those were under the age of one month. However, in another report[10], limited to children, a total of 18 cases were mentioned of which nine (including the author's case) occurred in the newborn.

In view of the relative rarity of this condition it would be appropriate to add the present case which is the first recorded in one of Negro newborn twins.

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CASE REPORT

H. W. (Baby B), a premature male infant, was a breech delivery at 2:55 P.M. on July 23, 1946. He was the second of twins and weighed 4 pounds 10½ ounces. He breathed spontaneously, cried vigorously at birth, and no physical abnormalities were noted. On the day after birth, he began to regurgitate. Examination at this time revealed a normal temperature, depressed fontanels, increased but regular rate of respiration, distended abdomen and some edema of the scrotum, penis, thighs and feet. On July 25, the fontanels were no longer depressed, the edema of the thighs and scrotum had decreased and the abdominal distention had disappeared. Two days later, the temperature suddenly rose to 39.4° C., the infant became lethargic and his respiration shallow. Dullness and fine moist râles were audible over the right lower lobe and the left axilla. His skin turgor appeared normal, and no alteration was noted in the tension of the fontanels. A diagnosis of bronchopneumonia was made. A combination of sulfadiazine and sulfathiazole, .1 Gm. of each per pound of body weight, was given once and then .03 Gm. per pound of each every four hours. By 6 P.M. the respirations had become irregular, a considerable amount of mucus was aspirated from the upper respiratory tract, and sternal retractions were noted with every third or fourth breath. In addition, two loose greenish-yellow stools had been noted. In view of the severity of the illness, in addition to the sulfonamides, penicillin was administered at once and then every three hours. Respirations became regular again and the general condition improved. On July 28 the temperature was still elevated, the chest findings were unchanged, the color was poor and one loose green stool was noted. From then until the next morning, the infant had three loose watery stools. The temperature persisted but no further respiratory distress was noted. However, at 12:30 P.M. the patient suddenly ceased breathing, efforts at resuscitation were unsuccessful and the infant was pronounced dead.

At *autopsy* the findings were:

1. Brain: The fontanels were not under pressure. There was slight increase in the cerebral spinal fluid. Both hemispheres were covered by localized areas of pus. The base of the brain near

the medulla disclosed a few similar areas. These areas varied from the size of a ten to fifty cent piece. There was also marked congestion of the brain and the ventricles contained a small amount of fluid. Bacteriological examination of the purulent material revealed Friedlander's pneumobacillus.

2. Lungs: Both were dark purple, hard in consistency and sank in toto when placed in water. On section, they showed a dark purple color and marked congestion.

3. Liver: Was moderately hard in consistency. The cut surface disclosed a mushy, dark red appearance with a yellowish tinge.

4. Spleen: Showed a wrinkling of the capsule. The surface was dark purple. On section, the spleen was mushy and the malpighian corpuscles were not prominent.

Post-mortem Diagnosis was:

1. Friedlander's bacillus meningitis.
2. Atelectasis of lungs.
3. Acute splenitis and hepatitis.

RÉSUMÉ OF THE FIRST INFANT'S COURSE

H. W. (Baby A), premature colored male infant, was a vertex presentation delivered at 2:50 P.M. on July 23, 1946. He was the first of twins and weighed 3 pounds 14½ ounces at birth. He breathed spontaneously, cried vigorously, and was placed in the premature nursery in good condition. He received the same routine as Baby B. He progressed well, there being no initial weight loss, and on September 10, 1946 he was discharged in good condition weighing 6 pounds 5 ounces.

Laboratory Work done on Baby A:

July 30, 1946: Nose and throat culture revealed staphylococcus aureus.

July 31, 1946: Lumbar puncture—spinal fluid negative.

August 2, 1946: Lumbar puncture—spinal fluid negative.

August 30, 1946: X-ray of bones—no bony pathology.

Other pertinent check-ups: Nose and throat cultures on both parents revealed staphylococci. Similar examination of the personnel in the delivery room and premature nursery failed to reveal any Friedlander's carriers.

TABLE 1. *Cases Occurring Up To One Month of Age*

Authority	Sex	Age	Associated Condition	Outcome
1. Schieb[11] (1900)	—	Infant	Otitis media	Died
2. Beitzke[12] (1904)	M	3 wks.		Died
3. Lequeux[13] (1905)	—	4 days	Omphalitis	Died
4. Bonhoff & Esch[14] (1912)	—	5 days	Otitis media, old hemorrhages in frontal & parietal lobes	Died
5. Elias[15] (1924)	M	7 days	Pneumonia	Died
6. Debré, Semelaigne & Lelong[16] (1930)	—	21 days	Bronchopneumonia & hydrocephalus	Died
7. Debré, Breca & Beros[17] (1930)	—	6 days	Suppurative hematoma of left parietal region	?
8. Babonneix & Riom[18] (1933)	—	5 days	Hydrocephalus	Died
9. Fothergill & Sweet[19] (1933)	M	4 wks.		Died
10. Davis & Fernando[20] (1935) Case 2	M	1 mo.	Pneumonia	Died
11. Slobozianu & Ianescu[10] (1940)	F	Newborn	Pneumonia & cerebral hemorrhage	?
12. Present case	M	4 days	Gastro-enteritis	Died

TABLE 2. *Cases Occurring Between One Month and Twelve Months*

Authority	Sex	Age	Associated Conditions	Outcome
1. Dufort, Delattre & Bonnet[21] (1926)	—	9 mos.	Arthritis of ankle and elbow	Died
2. Papandrea[22] (1927) Case 1	F	5 mos.	Pleuritis and pericarditis	Died
3. Bocca, Ranque & Senez[23] (1928)	—	2 mos.		Died
4. Moritz[24] (1936)	F	4 mos.	Mixed infection with TBC	Died
5. Leonhardt, Boucemont & Balmes[25] (1937)	M	4½ mos.	Bronchopneumonia	Died
6. Nobécourt[26] (1938)	M	8½ mos.		Died
7. King[27] (1946)	M	6 mos.	Bronchopneumonia and ileocolitis	Died

DISCUSSION

ETIOLOGY

1. *Age.* Of the cases reported in children, the majority occurred under one year of age with the greatest concentration of cases in the first month. In reviewing those listed in the literature, including the present case, 12 occurred in the first month, 7 between one and twelve months and only 6 from one to thirteen years of age. These results are given in Tables 1, 2 and 3.

TABLE 3. *Cases Occurring Between One and Thirteen Years*

Authority	Sex	Age	Associated Conditions	Outcome
1. Papandrea[22] (1927) Case 2	M	2½ yrs.		Died
2. Schiavene & Idelsohn[28] (1934)	F	4 yrs.	Followed surgical removal of cyst of upper eyelid	Died
3. Leonhardt, Boucemont & Balmes[25] (1937)	M	1½ yrs.	Injury to head	Died
4. Lombard & Lemaire[29] (1938)	M	7 yrs.	Injury to head and left tibia	Recovered
5. Montea & Real[30] (1940)	M	2 yrs.	Otitis and naso-pharyngitis	Recovered
6. Mori[31] (1943)	M	26 mos.		Recovered

TABLE 4. *Sexual Distribution of Cases in Children*

Age	Male	Female	Not Specified
Up to 1 month	5	1	6
1 to 12 months	3	2	2
1 to 13 years	5	1	0
Totals	13	4	8

2. *Color.* Until the present study, all cases in children had been recorded in the white race, and this is the first one reported in a Negro infant which was one of twins. However, in adults[5, 7] there had previously been reported three cases in Negroes and two in Chinese.

3. *Sex.* This condition has been reported[3] as occurring twice as often in males as compared to females. In this series, the males

have outnumbered the females by a 3:1 ratio as illustrated in Table 4.

4. *Focus of Origin.* As a predisposing cause, debilitating conditions[5, 7], such as diabetes, tuberculosis, syphilis and prematurity (as in the present case) may be factors.

The primary focus[5, 7, 10, 32, 33] may be found in infections of the pharynx, middle ear, mastoids, sinuses, lungs, joints or umbilicus. Furthermore, the bacillus is said to be found in the normal upper respiratory tract in from 1 to 5.8 per cent[34, 35] with its localization most often in the tonsils. Moreover, it has also been found to be a fairly common inhabitant of the intestinal tract and Dudgeon[36] found it in 5.5 per cent of feces of normal and abnormal individuals while Kendall[37] felt it was almost a constant inhabitant of the intestinal tract of nurslings and bottle-fed babies. Since, in many of the younger cases, no primary site[7, 38] of invasion could be demonstrated, it is possible that these normal nests of Friedlander's bacilli may have been the site from which the active infection originated.

In the present case, there was evidence of a gastro-intestinal disturbance on the second day which later was followed by diarrhea. It is very possible that this may have been the site of origin for the Friedlander's bacillus infection. In partial substantiation of this are several reports[39, 40] of epidemic diarrhea in the newborn which were caused by this organism but in these series no meningeal involvement was observed.

Other possible sources[8, 10] for this infection in the newborn are:

A. Hematogenous route, provided the mother had had a similar infection during her last month of pregnancy, of which there was no history in this case.

B. During birth from (1) amniotic fluid; (2) fingers inserted into mouth to clear away any obstructing mucus; (3) nasal and oral secretions of attendants.

In this case it was not necessary to do manual extraction of mucus, and bacteriologic examinations of the secretions of attendants were negative, which eliminates these two possibilities. However, it is conceivable that, since this was the second of twins and a breech delivery, he may have swallowed some amniotic fluid which resulted in a gastro-intestinal condition with increased

permeability of the mucous membrane associated with a probable hematogenous spread of Friedlander's bacillus to the meninges.

ASSOCIATED CONDITIONS

Friedlander's bacillus[1, 41] may be associated with suppurative processes in any part of the body, especially in the gastro-intestinal, genito-urinary and biliary systems.

Although diabetes[5,7] has been frequently associated with this condition in adults, in children intracranial hemorrhages,[10, 14] head injuries,[17, 25, 29] congenital syphilis[12, 22] and tuberculosis[24] were

TABLE 5. *Conditions Associated With Friedlander's Meningitis*

	Condition	Under 1 month	1-12 months	1-13 years
1.	Cerebral	5	..	..
	a) Hydrocephalus	2	..	..
	b) Cerebral hemorrhage	2	..	..
	c) Injury to head	1	..	2
2.	Pneumonia	5	..	..
3.	Otitis media	2	..	1
4.	Omphalitis	1	..	..
5.	Pleuritis	..	1	..
6.	Pericarditis	..	1	..
7.	Arthritis	..	..	..
8.	Gastro-enteritis	1	1	..
9.	Following surgery	..	..	1
10.	Mixed infection with TBC	..	1	..
11.	Congenital syphilis	1	1	..

found. In this series, the associated conditions that were noted are listed in Table 5.

DIAGNOSIS

Since, as in the present case, the usual signs and symptoms of meningitis may be lacking in infants[9, 28] the diagnosis must rest on the finding of the organism[5] in the spinal fluid. However, it must be remembered that even in some of the positive cases, the first spinal smear[5,7] may be negative so that in a suspicious case it may be necessary to do repeated spinal examinations. Moreover, the finding of Friedlander's bacillus in extrameningeal foci may suggest the diagnosis. Similarly, a positive blood culture facilitates the diagnosis and classifies the case as one of extreme severity.[5] Certainly, it is a condition to be kept in mind, especially in infants under one year of age, and even more so for those in the neonatal period.

TREATMENT

This type of meningitis is one of the most virulent and malignant so that until recently its diagnosis was almost synonymous with the sign of death.

Of the definitely incontestable cases, one[12] was reported as cured following operation. Others have reported successful treatment with prontosil,[29] sulfapyridine,[30, 32] sulfathiazole[31] and sulfadiazine.[43, 44] In Friedlander's bacillus septicemia, success has been attributed to sulfanilamide,[45] sulfadiazine[46, 47] and penicillin.[5, 48] On the other hand, sulfanilamide,[7] sulfapyridine,[46] sulfadiazine[27] and penicillin have been reported as ineffective in other cases. Experimental studies have shown that sulfanilamide[49, 53] was ineffective against the bacillus while sulfapyridine[46, 49, 50] exhibited moderate activity and sulfadiazine[51] seemed to be the best. Several reports,[52-54] including that of the Council on Pharmacy and Chemistry,[55] listed penicillin as ineffective against Klebsiella pneumoniae. More recently, streptomycin[56-63] has been reported as being the most effective agent against Friedlander's bacillus infections. Therefore, it should be the drug of choice as soon as the diagosis is made and should be given in large enough doses[60] and over a sufficient period of time.

SUMMARY AND CONCLUSION

1. A case of Friedlander's bacillus meningitis in one of Negro premature twins is reported.

2. A review of the literature revealed that half of the cases in children occurred during the neonatal period.

3. Males were affected three times as often as females.

4. In children, the condition most commonly associated with Friedlander's bacillus meningitis were cerebral lesions, pneumonia, congenital syphilis, otitis media, gastro-enteritis, omphalitis, arthritis, pleuritis and pericarditis.

5. The diagnosis is exceedingly difficult in early infancy, since there may be very few symptoms referable to the meninges. However, it should be considered in every case of unexplained fever associated with bulging fontanel, convulsions, vomiting or diarrhea and irregularity in rate or intensity of respiration.

6. Sulfonamides combined with penicillin were ineffective in this case.

7. Streptomycin at present is the drug of choice for this condition.

8. With the advent of antibiotics as effective remedies comes the added responsibility of diagnosing these cases as early as possible so as to extend to the unfortunate patient the full value of modern medical advances. In view of that conclusion, it must be cautioned that wherever the slightest doubt exists as to its presence a spinal tap must be done without hesitancy or delay, otherwise death may be the price to pay. Therefore when puzzled or in doubt, it is better to do another spinal tap needlessly than to have need of one hopelessly.

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ELECTROENCEPHALOGRAPHY IN DIAGNOSIS OF EPILEPSY IN CHILDREN. (Semaine des Hôpitaux de Paris, 24: 1609, July 2, 1948). Cornil and his co-workers made electroencephalograms of 184 children between the ages of 6 and 13 years, 138 of whom had clinical epilepsy, while in 46 the epilepsy was doubtful from the clinical point of view. A typically normal tracing, taking into account the age of the child, furnishes a presumption against the diagnosis of epilepsy, but does not provide definite proof. Positive diagnosis is made in the presence of two conditions: (1) when during rest one observes paroxysmal waves characterized by considerable amplitude, by their rhythmicity and sometimes by their regularity. Jasper's term of "hypersynchronic rhythm" seems to be appropriate because these rhythms are very likely due to an excessive synchronization of the cortical neurons; (2) when one observes a slow dysrhythmia which is incompatible with the age of the patient, in a child with nervous attacks of a definite or nearly definite epileptic nature. Electroencephalographic confirmation of the diagnosis of epilepsy was obtained in 90 per cent of the patients in whom clinical diagnosis of epilepsy was made. Probability of epilepsy is suggested every time when a definitely pathologic tracing has been obtained which is not specific for epilepsy in a child presenting nervous attacks the epileptic nature of which has not been established clinically. Such pathologic tracings are represented in general by a slow dysrhythmia incompatible with the age, or by continuous or paroxysmal slow hypersynchronous waves which may be elicited by hyperpnea in a child with considerable glycemia. The possibility of an epileptic process should be considered when one observes a pathologic nonspecific tracing in a child presenting nervous attacks whose epileptic nature appears unlikely from the clinical point of view.—*Journal A.M.A.*

PLASMA-OLAC FEEDINGS OF THE PREMATURE

Report of Two Cases

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In 1946 a preliminary report on neonatal feedings of oral plasma appeared in the literature.[1] In 1944 and 1946 other articles appeared discussing the use of synthetic amino acid mixtures in infant feeding with special emphasis on their use for the feeding of premature infants.[2, 3] Recently, a publication appeared which pointed out the advantage of high protein formulas for small prematures.[4]

During the past year we have been investigating, to a limited extent, the use of a synthetic amino acid mixture, and on two occasions we have had the opportunity to use a formula containing human plasma. We feel, because of the dearth of literature on the subject of oral plasma feeding, that these two cases are worthy of report.

CASE REPORTS

Case 1. This premature female infant was born April 12, 1947, in the twenty-sixth week of gestation, weighing 2 pounds 8 ounces. Immediate care of the infant was directed toward removal of mucus from nose and throat and conservation of body temperature. The infant was placed in an incubator where it remained, except for occasional out-of-the-incubator feedings and transfusions, until it was 54 days old. During this period oxygen therapy was continuous for the first 22 days of life. Carbon dioxide and oxygen were given for five minutes every four hours until the infant was two days old.

The infant received 2½ mg. of vitamin K every four hours for four doses during the first day of life, then 2½ mg. of vitamin K twice a day until the twenty-second day. Vi Penta, 8 drops a day, was started on the twenty-second day. Oleum Percomorphum was started on the twenty-third day. Elixir of Feosol, 8 drops a day, was started on the twenty-sixth day. These were continued throughout the remainder of the infant's hospital stay.

The infant developed a slight jaundice two days after delivery, which persisted for 23 days. During the infant's stay in the hospital there was only one period of cyanosis, which occurred during a feeding on the eleventh day of life. The infant passed three to five stools per twenty-four hour period. These were dark brown in color, gelatinous in nature, with a foul odor. The nature and odor of these stools were believed to be the result of the type of feeding used in this case.

Red cell counts and hemoglobin determinations were done almost every other day and transfusions were based upon the results of these blood counts. During the infant's stay in the hospital, it received seven transfusions of whole blood. The infant also received a solution of equal parts of plasma and 5 per cent glucose in normal saline subcutaneously daily at the rate of 10 cc. per pound of body weight for the first twenty-one days.

The infant's feeding schedule was as follows: Nothing by mouth for the first twenty-four hours. For the next twenty-four hours, a solution of half 5% Dextri-Maltose water and half plasma was given orally by dropper, one cc. every two hours. For the following three days, the infant was fed a half-and-half mixture of 5% Dextri-Maltose water and plasma every two hours in amounts from 1½ to 3 cc. From the fifth to the forty-third day the infant received a formula composed of plasma, water and Olac, providing 60 calories per pound of body weight. Plasma was maintained constantly at the rate of 120 cc. per day with water and Olac added to make a solution in the ratio of one tablespoon of Olac to two ounces of liquid. The amount per feeding was slowly increased over this period, and the feeding schedule was changed to a three-hour and finally a four-hour schedule. After the forty-third day, the formula consisted only of Olac and water in the ratio of one tablespoon of Olac to two ounces of water.

The infant's stay in the hospital was sixty-five days. On discharge she weighed 5 pounds 3¼ ounces. At no time during the hospital stay was there any evidence of regurgitation or vomiting.

Case 2. This premature male infant was born on April 30, 1947, weighing 3 pounds 7 ounces. The infant was placed in an incubator after delivery, where it remained until it was 35 days old. Continuous oxygen was given together with carbon dioxide and oxygen for five minutes every four hours for the first twenty-four hours.

The infant developed a slight jaundice at the end of the first week, which persisted for two weeks. There were no periods of cyanosis during the entire hospital stay. The infant had three to four stools daily, which were dark brown in color, gelatinous in nature, and foul in odor.

The infant received 2½ mg. of vitamin K every four hours for four doses during the first twenty-four hours, then 2½ mg. twice daily for the next twenty-one days. At the age of 23 days, Oleum Percomorphum was started and at twenty-six days Vi Penta was started. Elixir of Feosol was started at the age of thirty days.

Red cell counts and hemglobin determinations were done every other day and transfusions were based on the results of these tests. During the infant's stay in the hospital, it received five transfusions of whole blood. The infant also received daily a solution of ⅓ saline, ⅓ plasma and ⅓ Dextrose Lactate Ringers subcutaneously at the rate of 10 cc. per pound of body weight. The subcutaneous fluids were discontinued after three weeks.

The infant's feeding schedule was as follows: Nothing by mouth for the first twenty-four hours. The infant was then placed on a formula of Olac, plasma and water, as described in Case 1. The 5% Dextri-Maltose-plasma feedings were not used. When the infant was 21 days old, it developed a mild nasopharyngitis with a marked mucous discharge on both sides of the nares. During this period the infant refused plasma feedings, regurgitated frequently, and, as a result, the plasma was discontinued from the formula on the twenty-sixth day of life, at which time the infant weighed four pounds. During the same period the infant received 3,000 units of penicillin intramuscularly every three hours until all signs of the upper respiratory infection had cleared. Olac, 1 tablespoon, to two ounces of water was used for feeding during the remainder of the infant's hospital stay. Dextri-Maltose was added to the formula in necessary amounts and the infant was gradually changed from a three to a four-hour schedule. The infant was discharged on the fiftieth hospital day weighing 5 pounds 4½ ounces.

DISCUSSION

It has been our experience that plasma feedings in the premature cause the passage of dark brown, gelatinous, foul smelling stools.

These stools return to "normal" within 24 to 48 hours after plasma is removed from the formula.

It was also noted that when the formula was made up of half plasma, half water and Olac, that the formula would gel when placed in the refrigerator. For this reason, it was necessary to add the plasma to each bottle just prior to feeding.

We were also impressed with the lack of cyanosis in these two cases.

While this type of feeding is expensive, and not necessarily indicated as a routine for all premature infants, we feel that it is of definite value in the case of the very small premature infant.

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CONNECTION BETWEEN HEPATIC AND SKELETAL DEFECTS. (Maandschrift voor Kindergeneeskunde, Leyden, 16: 33, Feb. 1948). According to de Roever-Bonnet malformations of the skeleton are met with in different types of hepatic disease. These skeletal disturbances occasionally resemble rickets clinically as well as roentgenologically. Results of animal experiments indicate that the presence of bile is necessary for the absorption of vitamin D in the intestine and that the liver plays an important part in the internal metabolism of vitamin D. It is probable that the liver also exerts a special influence on the metabolism of calcium. In a boy aged 15 who had been well up to the age of 14 cirrhosis of the liver was accompanied by osteoporosis. The second patient had been hospitalized for the first time in 1928 as an infant aged 9 months, with symptoms of hepatomegalia glycogenica. In later years he was repeatedly hospitalized on account of hepatic and osseous lesions. He is now 21 years of age and manifests an osteoporosis that has existed for years. The author concludes that in the presence of chronic parenchymatous disease of the liver attention must be paid to the development of osteoporosis, which requires special treatment.—*Journal A.M.A.*

CLINICAL REVIEWS

In order to encourage the writing of clinical articles by recent graduates or senior medical students, the ARCHIVES *will publish monthly at least one such paper from the classes of Doctor Reuel A. Benson, New York Medical College, New York; Doctor Philip Moen Stimson, Cornell Medical School, New York, and Doctor John A. Toomey, Western Reserve University Medical School, Cleveland. Other interested medical schools are cordially invited to submit student papers for consideration.*

TUBEROUS SCLEROSIS*

REPORT OF CASE

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Tuberous sclerosis is a rare congenital disease characterized in its classic form, epiloia, by epilepsy, mental-defectiveness and adenoma sebaceum. Only sixty cases had been reported in the literature by 1912. It occurs in both males and females; it is apparently confined to the European races and is rarely found in the colored races; it is fairly common in Great Britain but is rare in the United States. The anatomical changes begin in intrauterine life and the onset is usually in the first two years, but may be delayed until puberty or even early adult life. The earlier the onset the more severe the disease and the shorter its course. Both familial and hereditary tendencies are present, but the condition can appear sporadically. The family history may show tuberous sclerosis, epilepsy or other mental taint, or it may be completely negative. It seems that children of young parents are more often affected than offspring of elderly parents; the position of the patient in the line of offspring is not important.

The disease was first described by Bourneville and Brissaud in 1880, and is sometimes called Bourneville's disease. The etiology is unknown. It is generally regarded as a congenital dysplasia, but has been termed neoplastic, and sometimes true neoplasms do appear, although the tendency is for very slow growth, if any, of the tumors. Neurofibromatosis may be closely associated, and the two diseases may coexist.

Pathologically, the dura may be thickened, but disturbances in the convolutions are not commonly found. Examination of the

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brain shows sclerotic nodules in the cortex and in the ventricles, particularly the lateral ventricles. The nodules contain glial cells and fibers and around this gliosis the nerve cells are disoriented, atrophied and reduced in number, and multinucleated nerve cells are found. The nodules often become calcified and cystic degeneration may be present. In the ventricles, especially in the floor, small nodules sometimes become confluent, giving the surface an irregular appearance, called "candle gutterings." The area between the caudate nucleus and the thalamus is a favorite site for the "candle gutterings." The nodules in the brain may go on to tumor formation, most often glioblastoma multiforme. They may cause hydrocephalus. In the eye, retinal nodes or phacomata are found, consisting of white or greyish irregularly rounded masses, usually multiple, and often overlying the disc. These may also become calcified or show cystic degeneration. They rarely grow, or, if they do, it is very slowly. They are found less commonly than are nodules in the brain and adenoma sebaceum of the face. Rhabdomyomata are sometimes found in the heart, and congenital tumors in the kidneys or other organs. The adenoma sebaceum is most usually in butterfly distribution on the face, and is much more marked at the nasolabial folds. This is not a true adenoma sebaceum but is composed mainly of connective tissue and capillaries. It becomes more prominent as adolescence approaches, with the normal stimulus to growth of the glands. Subungual fibromatosis may also be present.

Clinically, the first symptom to appear is often epileptiform convulsions. They usually occur very early, but their appearance may be delayed until puberty or early adult life, or rarely they may be entirely absent. The convulsions vary as to frequency and periodicity and may consist of petit or grand mal, Jacksonian seizures or epileptic equivalents. Remissions may occur, often for long periods, or the patient may die in status epilepticus. The fits may occur thirty or more times a day, or only once or twice a year. One patient was reported as having had only one convulsion during his lifetime. Mental defectiveness may manifest itself as retarded development at times. These children are slow to walk and talk, and dentition is slow. Their physical development is retarded and they are underdeveloped and of poor physique. The low grade mentality progresses to imbecility or idiocy, and

they soon degenerate to a purely vegetative state. Other children seem to develop normally and then intellectual deterioration and regression occur. Rarely, mental symptoms are absent. Psychic changes are prone to occur. Postepileptic mania may appear, or changes ranging from screaming and crying fits to a primitive type of catatonic schizophrenia, which often occurs at puberty, may appear. The psychic changes are progressive, and usually the child must be institutionalized. Neurological manifestations may or may not be present. The reflexes may be increased, decreased, absent, or completely normal. Rarely hemiplegia or diplegia occur. Muscular hypotonia in young children may progress to rigidity as they grow older. Dysarthria may be present from the beginning or may appear after the child has begun to talk more or less normally. Stigmata of degeneration, such as simian hand, are often present. Hydrocephalus is often observed.

Adenoma sebaceum is one of the more common signs of tuberous sclerosis. It may appear in early childhood or even in infancy, but is most commonly noted at about five years of age, becoming more marked at puberty. Pinkish or yellowish papules are present in butterfly distribution on the face, and, as has been said, are most marked at the nasolabial folds. Telangiectasia may coexist. Other skin lesions are common. Peau de chagrin, a rough irregular area, usually found on the back, of thickened skin about the size of a biscuit has been observed. Patches of brown pigmentation are fairly common. Subungual fibromatosis is a frequently observed manifestation of the disease. Of the skin lesions, only adenoma sebaceuin, peau de chagrin and subungual fibromatosis can be considered diagnostic for tuberous sclerosis. The skin lesions usually do not cause symptoms.

Although phacomata can be the only manifestation of the disease process, they are less often found than the nodules in the brain or the lesions on the face. They may cause visual disturbances, or hemorrhages into the eye may occur from the rupture of small cysts, and optic atrophy and cataract formation have also been reported. Congential heart disease may be present, murmurs may be heard, and death can occur from sudden heart failure. The tumors in the kidneys or other viscera seldom cause symptoms or signs, although frequency, dysuria, and hematuria are possible, as are symptoms and signs from other organ tumors.

Diagnosis of epiloia is easy. The combination of epilepsy, mental defectiveness and adenoma sebaceum leaves no doubt in the mind of the clinician that he is dealing with a case of tuberous sclerosis. However, incomplete forms or formes frustes exist which run a different course and in which the diagnosis may easily be missed. The patient may be handicapped by only an occasional convulsion, and simple epilepsy is diagnosed. Adenoma sebaceum alone is hardly enough on which to base a diagnosis, but, combined with any of the other lesions, it is quite diagnostic. It may be found combined with brain nodules, or with retinal nodules. Mental deficiency may be only mild or absent, psychic changes do not necessarily occur. There is no parallelism between the degree of the epilepsy and the mental changes. X-ray plates of the skull may be of aid in diagnosis by showing calcified areas in the brain or the ventricles. Encephalograms may show distortion of the ventricles although they are seldom enlarged, or masses may be seen in the walls. Electroencephalography may reveal abnormalities which are not yet evident clinically, but they cannot be used alone to differentiate between epilepsy and tuberous sclerosis. Post-morten examination of course will clinch the diagnosis with discovery of the typical sclerotic nodules in the cortex.

The prognosis is poor. Often the disease process spurts at adolescence and the patient begins a downhill course from which there is no recovery. The disease is progressive and cannot be halted by any means now at our command. Treatment can be only symptomatic. If one large nodule is present in the brain, it may be removed surgically with some hope of relief. Otherwise, treatment of the conlvusions with the usual sedatives is all that can be accomplished. Marriage of the patient should be advised against since the disease has a hereditary tendency. Most patients do not live beyond the second decade unless the disease is very mild. Death usually occurs from intercurrent infections or from status epilepticus, but it may be caused by intracranial or visceral tumors or by sudden heart failure. Until we know more about the etiology of tuberous sclerosis, we cannot hope to do more than control the symptoms as much as possible and attempt to prevent further cases by forbidding marriage of tainted stock.

CASE REPORT

J. F., an eleven-year-old white girl, was sent to the Children's Center by the Court because her father was unable to care for her properly at home. Her mother was in a mental institution, diagnosis unknown. The father was well, as were two older siblings. In December 1946 the child complained of headaches and diplopia and was sent to Ophthalmology Clinic at Flower-Fifth Avenue Hospital. Externally the eyes were negative and visual acuity was not impaired. Examination of the right fundus revealed the presence of two masses, one just above and nasally to the disc, and a larger one below and temporally to the disc. The masses were flat and white, and no pigmentation was seen in them. The lower mass obscured the retinal vessels and projected forward into the vitreous. It was felt that these lesions were suggestive of tuberous sclerosis. The child was next seen in Dermatology Clinic where a diagnosis was made of sebaceous adenoma, rough type, with shiny papular lesions in butterfly distribution on the face. The patient states that she has had these lesions for as long as she can remember. The skin lesions were considered consistent with tuberous sclerosis. Neurological examination showed double vision on gaze to the right, slight enophthalmos on the left, and a slightly narrower palpebral fissure on the right side with a shallower nasolabial fold on the right than on the left. The ankle reflexes were hyperactive bilaterally with preponderance on the left. No definite diagnosis was made, and electroencephalography was advised. In August 1947, a sixteen lead electroencephalogram with monopolar and bipolar recordings was made. The record showed scattered 3 to 8 per second medium voltage activity in temporal, parietal and occipital positions. There were long runs of a ten per second occipital alpha. With bipolar recordings, focal signs were seen over the right occipital positions, less markedly on the left. The impression was that of a borderline abnormal record, with bi-occipital focus, more marked on the right, and a repeat examination was suggested, which was done in October 1947. It was similar to the first one, still mildly abnormal with slow waves appearing in the occipital areas and with the difference between the two sides less marked than before. It was suggested that examination be repeated in a year. X-ray of the skull

was negative, showing no abnormalities in the anteroposterior, posteroanterior and lateral positions. Examination in Cardiac Clinic disclosed a history of possible rheumatic fever a year before, the child stating that she had had pains in the joints of the left side and had remained in bed for five months. This history was not substantiated. A blowing systolic murmur was heard at the apex, radiating to the right. The electrocardiogram was essentially negative, with no definite abnormal findings and only a one plus right deviation. X-ray of the chest showed slight cardiac enlargement. Diagnosis was made of rheumatic fever, mitral insufficiency, class II b. Micro sedimentation rate was 5 mm., a normal reading. Urinalysis was negative. Re-examination in Ophthalmology Clinic showed no change in the condition of the lesions, no diplopia, and pale discs within normal limits with no edema.

This child has adenoma sebaceum, retinal nodules which are consistent with a diagnosis of phacoma, a heart murmur which may be congenital or rheumatic in origin, and an abnormal electroencephalogram. Although she has had no epileptic convulsions or mental deterioration, the diagnosis is consistent with tuberous sclerosis. In the abence of mental and epileptic symptoms, the disease can be considered mild, and the prognosis fairly good. No treatment will .be instituted because she has no symptoms except diplopia and headache, which have disappeared, but she will be observed for further progress.

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REVIEW OF THE LITERATURE

THE EPIDEMIOLOGY OF POLIOMYELITIS*

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Acute anterior poliomyelitis is an infectious disease of childhood, which has stimulated the curiosity of more investigators, evoked more popular response in the form of funds-raising, and ridden with fear the minds of more anxious parents than any other childhood disease of today.

The capricious behavior of this disease tests the acumen of the clinician as well as the investigator. In its mildest form, it is probably a very common clinical entity but the full extent of its prevalence defies accurate evaluation. Its classically described manifestations represent a relatively less common, but depressingly tragic, form of the disease.

In general, it is not an important cause of mortality, its morbidity is not accurately known, but the seriousness of the damage it can produce in the unfortunate few, and the anxiety it evokes, justify the interest it has stimulated.

CLINICAL RECOGNITION

In general, poliomyelitis is characterized by fever, headaches, prostration, gastro-intestinal symptoms (vomiting, diarrhea), muscular pain, weakness and tenderness.

On physical examination, muscle spasm may be manifested by a cup-like depression under the clavicles, claw-hand, lordosis, knock-knees and increased resistence to passive stretch. Muscle weakness is recognized as reluctance and loss of power to active motion. One of the classic signs may be elicited by asking the patient to sit up, whereupon his head falls backward. In some cases, fasciculation and coarse tremors are present. Vasomotor phenomena, cutaneous hyperesthesia and deep muscle tenderness may be found. Signs of menigismus are a common finding. Early in the course, the tendon reflexes are irregular, but they disappear in completely denervated muscle.

*In September 1948 this essay was awarded first prize by Philip Moen Stimson, M.D., in a competition open to his third year students at the Cornell University Medical College for theses on a subject in the general field of contagion in children. Mr. Davolos will receive his M.D. in June 1949.

In the spinal paralytic form, which has been described above, urinary bladder retention may occur.

Bulbar poliomyelitis is characterized by involvement of any or all of the cranial nerve centers in the medulla (Cr. VII-XII), such as facial palsy, blurred speech, immobility or deviation of the palate, nasal regurgitation of fluids, deviation of the tongue, absent cough and gag reflexes. If the cardiac center is involved, the pulse is thin, rapid and irregular and the blood pressure decreased. Involvement of the respiratory center produces shallow rapid irregular jerky respiration. Usually the patient appears less toxic than with the spinal form.

Encephalitic poliomyelitis may present itself with any of the above symptoms and signs, plus coma. In a few cases, excitability, hyperirritability or convulsion may occur.

The most important laboratory aid is the lumbar puncture. The spinal fluid pressure is increased, the fluid may be hazy, and the sugar and globulin may be increased, and there is very commonly a leukocytosis, chiefly in the lymphocytes, of from 15 to 500 cells. These findings usually persist for about 10 days after the onset of symptoms. However there is no diagnostic laboratory test.[1]

Abortive poliomyelitis, which is very important epidemiologically though of less importance clinically, presents a very difficult problem in diagnosis. Some authors characterize abortive poliomyelitis as an acute febrile episode, usually associated with vomiting, headache and sore throat, lasting 24 to 36 hours, after which the child has malaise for several days.[2]

ETIOLOGICAL AGENT

The etiological agent of poliomyelitis is a well established entity. The characteristic clinical and pathological changes of this disease process can readily be produced by inoculation into monkeys, through suitable routes, of bacteria-free filtrates of spinal cord emulsions from fatal cases. This demonstration of the poliomyelitis virus was first performed in 1908-9 by Landsteiner and Popper and has since been duplicated repeatedly.[3] Dr. Rosenau has long advocated the etiological significance of pleomorphic streptococci, and, indeed, streptococci have been isolated from patients' spinal cords. However, the evidence in favor of the viral etiology is overwhelming and there is no reason for believing that streptococci are essential to the production of this disease.

In considering the properties of the virus of poliomyelitis, it should be borne in mind that various different strains are known to exist and that in all probability an even greater variety of strains than have already been studied exist.

By refined ultracentrifugation techniques, the size of the virus has been variously estimated between 8 and 25 millimicra.[3] This corresponds quite well with that established for two well-known strains (Lancing and MV) by electron microscopy as 12-34 millimicra. Electron microscopy, however, reveals no specific morphology for this organism. It was further noted that the virus did not exhibit the phenomenon of streaming birefringens of flow. On chemical analysis of a carefully isolated specimen, it gave a weakly positive Millon's reaction (for protein) and strongly positive reaction for carbohydrate.[4]

The virus of acute anterior poliomyelitis is a rather resistent microorganism which can be preserved for years in 50 per cent glycerol, and remains viable in distilled water (in the dark and at room temperature) for between 25 and 114 days. The duration of viability in milk is somewhat longer.

However, moderately high concentrations of the virus can be destroyed by exposure to temperatures of 45-55° C. It is also susceptible to ultraviolet light, since it may be attenuated by exposures as brief as 5 seconds and destroyed by exposure for 30 to 60 seconds. The concentrations of chlorine required to render the virus nonviable are in excess of those feasible for drinking or even bathing water.[3]

Biologically, the virus possesses a specific neuronotropism;[5] or at least develops it after inoculation into the central nervous system of experimental animals. More specifically, it has a predilection for motor neurons.

In living patients, the virus may be demonstrated, in the acute stage of the disease, in the nasopharyngeal secretions and stools, more constantly in the latter, where it may persist for as long as seven or eight weeks.[6] There are two reports of the isolation of the virus from the blood stream of patients ante mortem.[6,7] But the rarity with which this finding has been reported and the difficulty with which it is demonstrated[7] suggest that blood stream invasion is not very common or certainly not very massive.

In constrast to the concept of specific neuronotropism, advocated

by Howe and Bodian, is the view held by some authors that poliomyelitis is a systemic infection and that central nervous system involvement is an uncommon complication thereof. However, the occurrence, indeed the predominance, of the abortive form of poliomyelitis is no contradiction to the neuronotropism of the virus, as was shown by recent animal experiments in which inoculated chimpanzees, that were asymptomatically excreting the virus in their stools, were found to have typical minimal spinal cord lesions at autopsy.[8] Furthermore, recent virus isolation studies reveal that when small concentrations of virus are inoculated intracerebrally into animals (such as mice, hamsters, cotton rats) no symptoms may appear, but upon subsequent inoculation of CNS tissues from these asymptomatic animals into fresh animals, the clinical and micropathological manifestations may appear after three such blind passages.[7]

However, the virus has been isolated from nonneural tissues in human fatal cases. Sabin and Ward[9] have isolated the virus from axillary and inguinal lymph nodes, specimen of combined lung, liver, spleen and kidney, pharyngeal mucosa, washed wall of ileum and colon, as well as central nervous tissues. It is most probable that the presence of virus in nonneural tissues represents only incidental invasion, except in the case of alimentary mucosa which probably represents local proliferation.

The problem of whether the virus of poliomyelitis is a systemic or central nervous system parasite might be resolved by consideration of the well-known ability of viruses to alter their tropisms. That is to say perhaps part of the virus colony that gains access to the gastro-intestinal tract alters its tropism and contents itself with gastro-intestinal tissues, while more successful cohorts gain access to the central nervous system, producing changes which vary within a very wide range, depending on the susceptibility of the host.

SOURCE OF INFECTION

There is no satisfactory evidence for the existence of a non-human reservoir as a source of infection. Efforts to demonstrate the virus in the spinal cords of paralyzed fowls and the stools of sick dogs, found in the vicinity of human cases, were unsuccessful.[10] The same was found to be true of feces from cows, pigs, chickens, calves and bulls, excreta of roaches and ants, central

nervous system and gastro-intestinal tracts of mice and rats associated with sporadic cases.[11]

The only known reservoir of infection is man.[12] The virus has been known to persist in the stools for six months.[13] It has also been demonstrated in the stools of paralytic and nonparalytic patients in the months of January and February.[14] Kessel and Moore[15] investigated the problem of carrier state in children admitted to a general hospital for tonsillectomy. They found that no less than 5 and possibly 15 out of the 136 patients had infectious

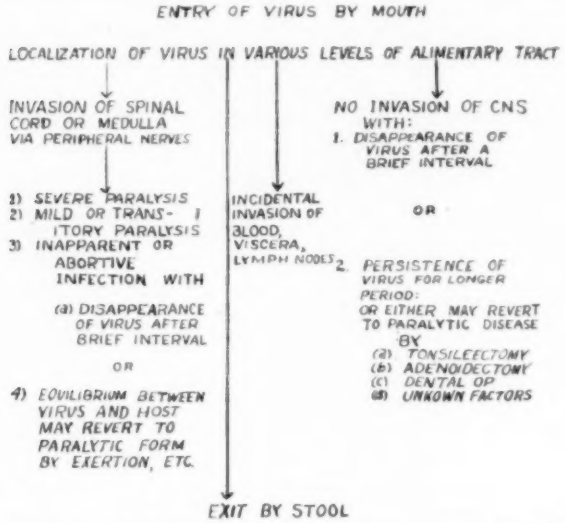
ENTRY OF VIRUS BY MOUTH
LOCALIZATION OF VIRUS IN VARIOUS LEVELS OF ALIMENTARY TRACT
INVASION OF SPINAL CORD OR MEDULLA VIA PERIPHERAL NERVES
1) SEVERE PARALYSIS
2) MILD OR TRANSITORY PARALYSIS
3) INAPPARENT OR ABORTIVE INFECTION WITH
(a) DISAPPEARANCE OF VIRUS AFTER BRIEF INTERVAL
OR
4) EQUILIBRIUM BETWEEN VIRUS AND HOST MAY REVERT TO PARALYTIC FORM BY EXERTION, ETC.
INCIDENTAL INVASION OF BLOOD, VISCERA, LYMPH NODES
NO INVASION OF CNS WITH:
1. DISAPPEARANCE OF VIRUS AFTER A BRIEF INTERVAL
OR
2. PERSISTENCE OF VIRUS FOR LONGER PERIOD:
OR EITHER MAY REVERT TO PARALYTIC DISEASE BY
(a) TONSILECTOMY
(b) ADENOIDECTOMY
(c) DENTAL OP
(d) UNKNOWN FACTORS
EXIT BY STOOL

Fig. 1. Hypothetical Behavior of Virus in Man. (From Sabin[60], Connecticut M. J., March 1945).

concentrations of virus in the excised tonsils, stools or both during an interepidemic period. None of these children had ever had poliomyelitis or even had known exposure.

Extensive virus detection studies during the Fort Worth, Texas epidemic (1943) revealed that the virus was frequently present in asymptomatic members of families in which there was household contact with clinical poliomyelitis, less frequently in non-household contacts, and even in families where no known contact had occurred.[16]

Therefore, it is clear that a carrier state exists. This carrier state may result from clinical infection—paralytic or abortive—contact with clinical cases, and possibly from contact with carriers. The preponderance of available evidence is strongly against the existence of any non-human reservoir, and indicates that the source of infections consists of human acute cases, convalescents and carriers, the virus being harbored in the throats and stools.

MODE OF TRANSMISSION

Numerous agents have been investigated as possible vectors which transmit the poliomyelitis virus. Even a superficial review of the literature readily reveals the extent of conflicting opinions.

Some of the reasons for the difficulties in this connection might briefly be mentioned. Foremost amongst these are the ubiquity of the virus and the wide variation in the degree of its clinical manifestations. The virus has been known to occur in water, sewage, flies, milk and people—all agents which offer extensive possibilities for dissemination.

Also, rather massive contamination of the gastro-intestinal tract can produce any clinical picture from no symptoms at all through gastro-intestinal disturbances to paralysis and death in different individuals. A symptomatic infection is by far the most common. Clearly, consideration only of those cases with sufficient clinical manifestations for a positive diagnosis is apt to present a grossly distorted epidemiological picture.

In establishing the mode of transmission, certain criteria may be set up in any given epidemic:

1. The virus should be demonstrable in the suspected vector.
2. Contact with the vector should be demonstrated for all the clinical and subclinical cases.
3. The occurrence of the epidemic should be preventable or the course significantly altered by eliminating the vector.

These criteria will serve a double purpose, since their satisfaction provides adequate evidence for establishing the suspected mode of transmission. And, if it could be demonstrated that any given vector could not possibly have satisfied any single one of these criteria, it is satisfactorily eliminated. This postulate is, of course, predicated on the assumption that there is only one mode of transmission which is operative to any important extent.

4. A fourth criterion might be considered namely that the epidemic curve should parallel that of other diseases transmitted by the same mechanism. This criterion is not as valuable as the others at the present time, since the difficulties in diagnosis of mild forms and the impossibility of clinically diagnosing the asyptomatic carriers which have been produced during the epidemic, make it difficult to obtain an accurate epidemic curve.

With these considerations in mind we may proceed to a discussion of some of the more commonly suspected vectors.

Water. The duration of viability of the virus in water and the resistance of the virus to routine concentrations of chlorine justifies the suspicions that have been entertained. Furthermore, the virus has frequently been isolated from sewage-contaminated waters.[17,18]

However, reports of epidemics which could definitely be traced to contaminated water supply are difficult to find in the literature. It has also been pointed out that the typical poliomyelitis epidemic lacks the characteristics of a water-borne epidemic, in which large numbers of people are infected more or less simultaneously and in which a common factor of contaminated water supply may be found to link the cases. On the contrary, poliomyelitis spreads slowly and radially; and in rural areas, it spreads at a regular rate regardless of the nature of the water supply.[19] Therefore, contamination of water supply or contact with contaminated bathing waters should be considered a possible or contributing factor in the transmission. But, it is probably not a common or important agent of transmission.

Milk. The virus of poliomyelitis has been demonstrated to remain viable in milk longer than in water, although it does not multiply. Milk is, therefore, a potential vehicle. Indeed, the analysis of one epidemic, which occurred in England, elicited circumstantial evidence that strongly suggested the epidemiological role of a contaminated milk supply. This epidemic, however, was hardly typical, since it began in the month of October, had a very sudden onset and a sudden decline. Also, only well-to-do individuals were afflicted, and all the cases were exposed to one grade of milk produced by one dairy in a community supplied by several dairies.[20] Such epidemics are rare, and it is unlikely that milk very frequently plays an important role.

Food. Many explanations have been offered for the highly specific seasonal incidence of poliomyelitis. Amongst these is the belief that fruits, possibly contaminated by flies, play a role in the transmission.

The virus has been isolated in infective concentrations from fruits.[21]

Although the typical poliomyelitis epidemic curve does not present the characterics of a food-borne epidemic, the analysis of a recent epidemic offers evidence to suggest the participation of contaminated fruit in that particular epidemic. In this study of 206 cases, all gave a history of having eaten unwashed fruit. Forty-five patients were members of families in which multiple cases occurred; 32 of these developed symptoms within 0 to 5 days of each other, suggesting simultaneous exposure.[17] However, the attempts to rule out other modes of transmission were not entirely satisfactory. For example, the authors rule out direct contact by the fact that the population was scattered and that direct contact with active cases could have been possible in only 13.6 per cent. This is hardly conclusive in view of the fact that the carrier rate in poliomyelitis is probably quite high during epidemics, and they have not considered this aspect of direct contact.

In any event, the evidence herein presented is certainly sufficient to justify demands for sanitary food handling, although contaminated food is probably not the most important vehicle.

Insects. The concurrent seasonal prevalence of poliomyelitis and insects has stimulated interest in the potential epidemiological role of insect vectors. The virus has been demonstrated to occur inside non-biting flies, such as blow flies and house flies.[22] It has been postulated that the flies carry the virus from contaminated feces and sewage to food.

It has been observed, however, that the virus can be found in flies regardless of the sanitary facilities and that epidemics have occurred where flies were not prevalent. The strongest evidence against insect transmission arises from a recent investigation into the influence of fly-abatement measures on the course of an epidemic. Two comparable urban areas were selected, and early in the course of the epidemic one was intensively sprayed with DDT. In the experimental area, the fly population was reduced to 10-25 per cent of the previous level, yet there was no significant

difference between the course of the epidemic in the experimental and the control areas. Similar, though less vigorous, measures were employed in another area after the peak of the epidemic had passed; again there was no significant alteration in the course of the epidemic.[23]

Since the virus has been isolated from flies, they should not be completely disregarded.

Direct Contact. By far the most convincing evidence has been

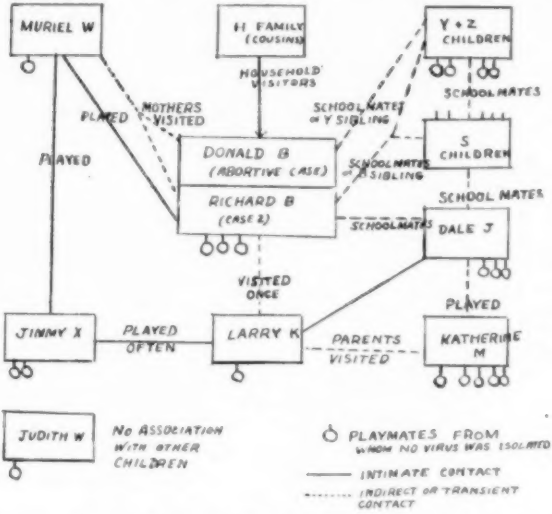

Fig. 2. Direct Contact in Poliomyelitis. Two cases of poliomyelitis in Three Oaks, Michigan, 1942. The stools of 282 people, including all children under the age of 16, were studied for the presence of virus. Direct contact of some degree was established for almost every person with the virus in his stools. Heavy lines indicate more intimate contact (from Pearson and Rendtorff,[11] Am. J. Hyg., 41: 179, 1945).

accumulated in favor of the transmission of poliomyelitis by direct contact. The virus has been isolated from nasopharyngeal secretions, tonsils and stools of active cases, convalescents and asymptomatic carriers, some of the latter having had no known contact with active cases.

In view of the prevalence of asymptomatic carriers resulting from contact and the prevalence of the abortive which is so difficult

of diagnosis clinically, it would appear that the extent and mode of spread of the virus might better be appreciated by virus isolation studies rather than by its clinical manifestations.

Such laboratory studies, following a single case occurring in a boys' camp, reveal the presence of the virus in the stools of five out of six boys exposed, but not in either the stools or the nasopharynx of boys that were not exposed.[24]

Similarly, the recent severe epidemic in Fort Worth, Texas (1943), was investigated, by extracting the stools of contacts and non-contacts for the virus. Using pools of stools from members of families (excluding the active cases), it was found that the virus could be demonstrated in: (1) 6 out of 8 (75 per cent) of the families in which active cases occurred. (2) 8 out of 45 (18 per cent) of the households in which known nonfamilial contact had occurred. (3) but in only 2 out of 127 households (1.6 per cent) in which no known contact had occurred.[16]

Thus there is a definite pattern in the distribution of the virus, the frequency being greatest in the immediate proximity of the clinical cases. This finding is confirmed by individual studies. For example, 20 out of 27 individuals (in 4 different families) who had intimate contact with a paralytic case, had the virus in their stools, but the virus was not found in a family with no contact.[26] Nor are these results without duplication.[27,28]

In a study of sporadic cases, the virus was similarly found in relatives of paralytic cases but not in a large series of noncontacts.[11] Thus, the same pattern obtains and it is found in large and small towns alike.[29]

The radial spread of poliomyelitis has also been worked out by following the spread of clinical cases temporally and spatially from a known focus. The epidemic was known to have started with the exposure of two individuals to a paralytic case during the prodromal stage. In this study, the time period of the epidemic was divided into stages as follows: 1st stage—2 days after the onset of symptoms in the original case, representing the period during which the first case was infectious. 2nd to 7th stage—12 day periods, representing the average incubation period of poliomyelitis. 8th stage—2 twenty-four day periods.

Then, the average air line distance of the cases occurring in each stage from the site of the original case was determined. It

was well illustrated that as the epidemic progressed, the new cases occurred at progressively greater distances from the original case. This is demonstrated graphically in Fig. 3.[38]

The typical epidemic curve of poliomyelitis, which is illustrated

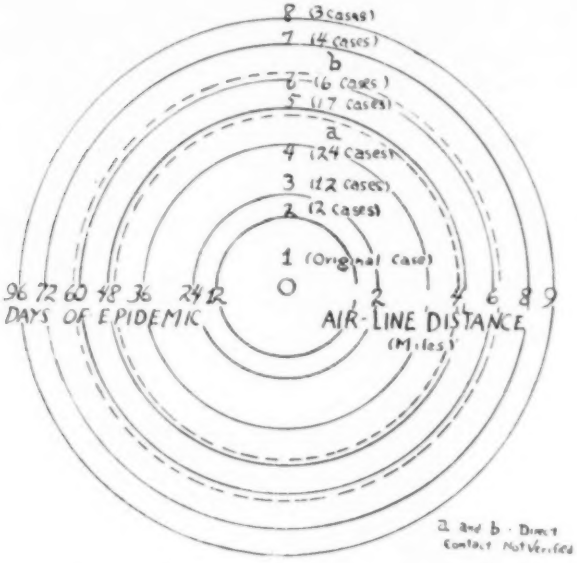

Fig. 3. Radial Spread in Poliomyelitis. Numbers to the left indicate the duration of the epidemic in days. Numbers to the right indicate the average air-line distances of cases occurring in the corresponding time intervals from the original case. Numbers extending upwards denote the periods into which the epidemic was divided on the basis of the average incubation period of poliomyelitis, 12 days. Next to these, in parentheses, are the numbers of cases that occurred. Direct contact, consisting of single or multiple exposure to infectious cases, was established for all except those at a and b. (From data in Casey,[39] Am. J. Dis. Child., 69: 152, 1945).

by the study cited above, is certainly consistent with spread by direct contact.

In retrospect, it may be seen that the evidence for transmission by direct contact satisfies more of the criteria discussed above and more convincingly that the evidence which has been presented

for other modes of transmission. Indeed, it satisfies adequately all but criterion 3, the satisfaction of which requires the achievement of the ultimate goal, namely, the control of epidemic poliomyelitis.

The specific mechanism by which poliomyelitis is spread is less well established. It is suggestive that the infectious period of the acute case[31] corresponds very closely with the period during which the virus is frequently found in the nasopharyngeal secretions several days before and several days after the onset of symptoms. It has also been reported that infection contracted from acute cases most often follows intimate contact of several hours duration—more intimate and prolonged contact than could occur with droplet exposure alone.

In addition, transmission by stools, as well as nasopharyngeal secretions, and by carriers and convalescents, as well as acute cases, very likely play an important role.

PORTAL OF ENTRY

Experimentally, the clinical and pathological changes of acute anterior poliomyelitis can be produced readily by inoculation of the virus into any of the body surfaces that are exposed to the external environment—the respiratory tract, gastro-intestinal tract and the skin. However, it is much more readily produced by intranasal or gastro-intestinal instillation. In human fatal poliomyelitis, the virus can frequently be isolated from the wall of the pharynx and small intestine, as well as from the nasopharyngeal secretions and stools. Hence, circumstantial evidence indicates that the gastro-intestinal, pharyngeal and nasal mucosal surfaces are the portals. However, more complete consideration reveals that the nasal mucosa is an unlikely portal in human poliomyelitis.

Howe and Bodian[5] have demonstrated quite conclusively, in a long series of carefully controlled experiments, the routes that the virus takes within the body. They found that the virus travels centripetally up peripheral nerves to gain access to the central nervous system, and within the central nervous system the virus utilizes definite accessible nerve tracts to approach parts of predilection. In monkeys, the nerve tracts chiefly used were the reticulospinal, corticospinal and olfactory and the parts predominantly attacked were the anterior horn cells of the cord, reticular formation, midbrain tegmentum, fields of Forel, motor cortex, hypo-

thalamus and the olfactory bulbs and associated centers.

Two autopsy series on human fatal cases, however, reveal no notable differences in the distribution of the central nervous system lesions, namely, that the olfactory bulbs and associated centers were not involved,[8,31] indicating that the olfactory nerves were not utilized and the nasal muscosa was not the portal of entry. This is supported by the fact that chemical block of the nasal mucosa does not produce significant protection against infection during an epidemic.

Thus, the pharyngeal and small intestinal mucosa are the most likely portals of entry.

INCUBATION PERIOD

Attempts to determine the incubation period by noting the time that elapses between the exposure to an active case and the onset of symptoms give a range of from 5 to 35 days, with an average of 12.8 + to 1.2 days.[32] In most cases, the interval appears to be one to two weeks.[31] Abortive poliomyelitis may have a somewhat shorter incubation.

PERIOD OF COMMUNICABILITY

As has been seen in the preceding discussion, transmission is most probably effected by direct contact with contaminated nasopharyngeal secretions and stools. In the active cases, the virus persists in the nasopharynx for about 4 days after the onset of symptoms,[20] and in the stools for about 2-3 weeks after the onset. The latter interval, therefore, represents the maximum period of communicability after the onset in most cases, although the virus may persist for 6 months or longer in some cases.

Clinico-epidemiological observations, on the other hand, in one study, reveal that infection has resulted from exposure during a period of from 3 days before to 3 days after the onset of prodromal symptoms. In other smaller series, the infectious period was found to extend from 4 days before to 5 days after the onset of symptoms. Although these latter studies are more concrete than the virus isolation studies, they are not sufficiently extensive to indicate the full range of the period of communicability. An individual should be considered potentially infectious so long as the virus is present in his throat or stools.

SUSCEPTIBILITY AND IMMUNITY

The classical principles of infection consider three factors: the number of organisms, the virulence of the organism and the resistance of the host. The one factor which appears to be of prime importance in poliomyelitis is the resistance, or susceptibility of the host.

Of all the individuals who become contaminated with infective doses of the virus during an epidemic, relatively few develop permanent or transient paralysis; probably more develop an acute febrile illness without sufficient central nervous system damage to produce any neurologic symptoms, and more yet develop no symptoms at all. It is clear from virus studies on the stools of paralytic cases and asymptomatic contacts that the virus is much more widely disseminated than the clinical disease is. There can be little doubt that susceptibility to the disease varies widely from person to person and that the susceptibility determines more than any other single factor the occurrence and the degree of the symptomatology.

Specific immunity, the immunity due to specific humeral antibodies which result from contact with the infectious agent, is far from well understood in poliomyelitis. The presence of antiviral substances in sera taken from people throughout the world and the reported higher incidence of poliomyelitis in rural adults over urban adults has led to the suggestion that resistance is attained by subclinical infection. However, more careful scrutiny exposes this belief to considerable doubt. Controlled studies on experimental animals reveal that virucidal antibodies are not always found in the sera of convalescent monkeys. When they do occur, they are not formed at a regular rate and are not maintained with any constancy. The animals did develop resistance, but re-inoculation did not increase the titre of antiviral antibodies in the serum.[35]

(To be concluded in February issue)

CLINICAL-PATHOLOGICAL CONFERENCE

WILLARD PARKER HOSPITAL, NEW YORK
Meeting held December 21, 1948
DR. PHILIP MOEN STIMSON, presiding.

PERTUSSIS ENCEPHALOPATHY

DR. SEPKOWITZ presented Case No. 5144, a 17-month-old white female, who was admitted to Willard Parker Hospital on November 4, 1948, at 11:30 P.M., for whooping cough and convulsions.

History of Present Illness. The patient was well until two weeks prior to admission when she developed a cold. On October 28, 1948, seven days before admission, she began to whoop and vomit. On the day of admission the mother noted some unusual twitchings of the patient's body. She then called her physician. The patient had four generalized convulsions the morning of admission. She received an injection of penicillin. About 6 P.M. she started to have more convulsions which became continuous.

On Admission the temperature was 102° F., pulse 160, respirations rapid and irregular. The patient was a well developed and well nourished female infant, acutely and desperately ill. The skin was mottled and cyanotic. The pupils were dilated and fixed. In the chest, râles were heard throughout both lung fields. The abdomen was markedly distended. A large amount of mucus was present in the nose and throat.

Hospital Course. The patient was given oxygen and suctioned. Phenobarbital, grain 1, was given intramuscularly; 10 minutes later phenobarbital, grain 1, was administered intravenously, into the femoral vein. The convulsions continued unchanged. The pulse was not palpable. The extremities turned cold and clammy. In 30 minutes, phenobarbital, grain 1, was given intramuscularly again. About 45 minutes after the initial dosage of phenobarbital, the patient ceased having convulsions, coughed and whooped a few times. Respirations became more regular, but the color remained unchanged. The pupils were less dilated, reacting slightly to light. However, the mottling soon increased. Breathing changed to irregular gasps, and the heart sounds became too rapid to count. Froth appeared in the mouth; the heart beat was no longer de-

tected. Coramine was then administered intramuscularly. Intravenous adrenalin produced a few gasps. The pupils were noted to be fixed again and the patient was pronounced dead at 1:20 A.M., one hour and 50 minutes after admission.

Autopsy Findings by Dr. Dolgopol. The body was that of a well developed baby girl of 17 months old. The left pupil was somewhat wider than the right. There was a moderate diastasis of the recti muscles but there was no herniation. The heart presented no abnormal findings; both diaphragmatic vaults were at the fourth ribs. The lungs were free; scattered areas of atelectasis were present in both lungs, mainly on the posterior aspects; there was no pneumonia. Other internal organs presented no abnormal findings. The brain weighed 1120 grams. It was very soft, moderately congested and markedly edematous with flattening of the convolutions, but there was no subarachnoid edema. The mastoids and middle ears showed no pathology. Microscopically the lungs were congested and showed numerous areas of partial atelectasis and some areas of emphysema, and a few alveoli contained groups of macrophages. The bronchial walls were markedly congested and infiltrated with lymphocytes, plasma cells and some polymorphonuclears. Leukocytes were present in the lumen of many bronchi. The liver showed no significant fatty changes. In the spleen, small hemorrhages were present in the pulp. The brain microscopically showed a moderate edema of the meninges and a considerable congestion of the brain substance. Plugs and clusters of lymphocytes were present in a number of capillaries in various parts of the brain, but there was no thrombosis seen in any blood vessels. Severe anoxemic changes were present in the ganglion cells in the motor cortex in the hippocampus, the thalamus and in a number of Purkinje's cells of the cerebellum. Those cells stained brightly with eosin and were almost colorless when stained with cresyl violet. These are common changes in the encephalopathy of pertussis. We did not succeed in isolating the H. pertussis from any other organs in the autopsy.

RAT-BITE FEVER

DR. ROBISON presented Case No. 5231, a 21-year-old Negro female, sent on November 21, 1948, as a case of measles from an-

other hospital with the following history which was obtained from the patient.

History of Present Illness. She stated that she was perfectly well until two weeks prior to admission at which time she began to have intermittent attacks of para-umbilical pain. A maculopapular rash appeared one week prior to admission and four days before admission the patient started vomiting. At this point she began to have fever. She was treated by her local physician and then referred for hospitalization when her condition did not improve.

On Admission here the temperature was 104° F., respirations 28, pulse 110. The patient was well developed and well nourished, lethargic, drowsy and markedly dehydrated, and responded to questioning incoherently. There was a maculopapular rash over the neck, arms and trunk which appeared confluent and in some areas of such intensity, especially over the extensor surfaces of the arms, that it was almost hemorrhagic. The skin was dehydrated with loss of turgor. The pupils reacted to light and accommodation and there was a mild conjunctivitis. The mucosa of both nostrils had small hemorrhagic areas. White areas were seen on the buccal mucosa interpreted by two observers as Koplik's spots, although they were larger than normal. The breath was not acidotic. There was a mild injection of the pharynx and no tonsillar pseudomembrane. The lungs were clear to auscultation and percussion. The heart sounds were distant, with a regular rhythm, and the blood pressure was 76/54. The abdomen was soft and no point tenderness nor masses were felt. The liver, kidneys and spleen were not palpable. Neurological examination revealed no stiffness of the neck. All deep reflexes were hypoactive. Abdominal reflexes were not elicited. Brudzinski, Kernig and Babinski signs were negative.

Vaginal examination revealed a soft cervix with an inflammed cervical canal and a moderate amount of yellow discharge. The urine was negative for sugar and a spinal tap was clear and had no cells. The impression at this point was measles encephalitis, with possible pelvic inflammatory disease. A hypodermoclysis was started at 1:00 A.M. Penicillin was given with supportive therapy. Three hours after admission the temperature rose to 107° F. Ice water enemas and sponging failed to lower the temperature below 103° F., after which it promptly went back to 106° F. The patient

became completely comatose, and expired at 5:25 A.M., six hours after hospitalization here.

Autopsy Findings by Dr. Dolgopol. The body was that of a well developed young colored woman. The entire body showed a diffuse macular morbilliform eruption which, on the upper part of the back and on the upper part of the extremities, was almost confluent and in places appeared to be slightly hemorrhagic. There were no signs of any local skin injury. Several large whitish spots were present on the buccal mucosa opposite the molar teeth. The sclerae were slightly yellowish but not definitely jaundiced. The pupils were in middilatation, but the left was slightly wider than the right. No bile pigments were found in the urine. A number of mesenteric peripancreatic, supraclavicular and cervical lymph nodes were found to be enlarged and congested. There was about 30 cc. of clear yellow fluid in the pericardial cavity, but the heart was not enlarged. The myocardium was pale and firm, and the right ventricle was moderately dilated. Both lungs were congested and showed scattered areas of atelectasis. A small patch of pneumonic consolidation was found in the left upper lobe. The liver was large, weighed 1,920 grams, was yellowish in color and quite friable. The spleen weighed 340 grams, appeared mottled on the surface, the pulp was greatly congested and soft and scraped readily.

The kidneys were normal in size, but the cortex was rather wide; the capsule stripped readily. The urinary bladder contained about 150 cc. of moderately concentrated urine. The fundus of the uterus showed a markedly congested endometruim. The brain appeared grossly normal and was not congested. The spinal cord appeared to be normal. Microscopically the heart showed some degeneration and fragmentation of muscle fibres. The consolidated areas of the left lung showed a peculiar pneumonia with macrophages and occasional giant cells in the alveolar lumen. The sections were negative for tubercle bacilli but contained a few spirilli. The liver contained multiple small foci of necrosis with an accumulation of pale cells with curved nuclei. These foci contained a few spirilli and some thin bacilli which were visible only on silver preparation. In the spleen the pulp contained numerous small abscess-like foci which contained similar organisms. Mesenteric lymph nodes also contained similar foci which had the same organisms. In the kidneys the tubular epithelium was markedly degenerated,

but there were no inflammatory necrotic foci. The brain showed no inflammatory changes but there were many degenerated cells in the oculomotor nuclei and in the reticular nuclei of the medulla. Some anoxemic changes were present in the Purkinje's cells of the cerebellum.

This is a case of an unusual spirillosis. The patient had a negative Mazzini test, so it is unlikely to be a case of syphilis. The pathological picture is not that of Weil's disease, as the histological picture of necrosis is not characteristic of that disease and there was no inflammatory infiltration in the kidneys. The only disease that shows focal necrosis in the spleen similar somewhat to our case is relapsing fever, which disease is very unusual in New York. We must consider the possibility of rat-bite fever acquired without the history of a rat-bite.

Second Attacks of Poliomyelitis. (Praxis, Bern, 36: 563, Aug. 14, 1947). Zellweger cites reports to the effect that second attacks of poliomyelitis are on the increase in recent years. He cites 38 reported instances of second attacks. Bridge, Clarke and Abbe observed symptoms indicative of inapparent poliomyelitis in persons who had had poliomyelitis previously. Second attack of poliomyelitis could be produced experimentally in animals. Animals contract poliomyelitis more readily a second time when they are infected with another strain of virus and by way of a different portal of entry than at the first attack. The existence of a specific humoral immunity is unlikely, but a local resistance exists at the portal of entry and in the nerve tracts which formerly had been in contact with the virus. It may also be assumed that a cellular immunity exists in the central nervous system. Presumably, every new poliomyelitis infection leads to a combat between the virus and the nervous tissue of the host. If the virus enters a second time through the same portal of entry, the host organism will usually be victorious owing to the local immunity, but even if the virus enters by a different route, a specific resistance of the central nervous system or some parts of it will have a favorable effect on the course of the disease.—*Journal A.M.A.*

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